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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
03/06/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/765,067	PAGE ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-10 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-10 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 07/777,730.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/12/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/12/2009 has been entered.

Applicant's amendment, filed 02/12/2009, has been entered.

Claims 1, 9 and 12 have been amended.

Claims 4-6 have been canceled.
Claims 2-3, 11 and 13-14 have been canceled previously.

Claims 1, 7-10 and 12 are pending.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Office Action will be in response to applicant's amendment, filed 02/12/2008.

The rejections of record can be found in the previous Office Actions, mailed 11/29/2006, 08/28/2007, 12/14/2007 and 08/13/2008.

3. Applicant Information Disclosure Statement (IDS), filed 02/12/2009 has been considered.

However, applicant should provide the dates of all of the references cited on the IDS.

4. Again, applicant's previous comments that the guidelines for the arrangement of the specification are merely guidelines and are not required have been acknowledged.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 7-10 and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the therapeutic indices of immunosuppressive drugs / biopharmaceutical drugs such as antibodies can be species- and model-dependent, it is not clear that reliance on the in vitro and in vivo experimental observations of certain antibody specificities accurately reflects the relative ability of any antibody / antibody specificity to treat a human patient suffering from rheumatoid arthritis encompassed by the claimed methods.

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Kahan clearly states that no in vitro immune assay predicts or correlates with in vivo immunosuppressive efficacy; there is no surrogate immune parameter as a basis of immunosuppressive efficacy and/or for dose extrapolation from in vitro systems to in vivo conditions (Cur. Opin. Immunol. 4: 553-560, 1992; see entire document, particularly page 558, column 2).

In reviewing Immunosuppressive Therapy of Autoimmune Diseases shortly after applicant's effective priority date, Bach (TIPS 14: 213-216, 1993) note the importance and limitations of whether the disease is B or T cell mediated, given the differences in sensitivity to intervention, of the role of target autoantigens and of the stage of the disease (see entire document). With respect to T cell mediated diseases such as arthritis, monoclonal anti-T cell antibodies were used in patients with rheumatoid arthritis, but it was premature to interpret such data (e.g., see T cell mediated diseases on page 215, column 1).

The specification does not adequately teach how to effectively treat rheumatoid arthritis by administering any antibody / antibody specificity. For example, the antibodies to the cancer cell markers CD33 and CD38 (e.g., see page 6, lines 2-3 of the instant specification) would not have been expected to treat arthritis. The specification does not teach how to extrapolate data obtained from certain antibody specificities (e.g., CDw52) (e.g., see page 5, paragraph 2 of the instant specification) to the development of effective in vivo human therapeutic methods to treat rheumatoid arthritis with any antibody specificity, commensurate in scope with the claimed invention.

There is insufficient objective evidence that the skilled artisan would predict that such a diverse class of compounds specific for various targets would be recognized as a single class of compounds.

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective therapy of rheumatoid arthritis with any antibody specificity, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for treating rheumatoid arthritis with any antibody specificity.

Applicant is invited to amend the claims to limit the antibodies to those antibody specificities that would be effective in the treatment of rheumatoid arthritis and to provide evidence accordingly.

7. Claims 1, 7-10, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adair et al. (EP 0388 151 A1) in view of Mather et al. (U.S. Patent No. 5,122,469), Zettlemeissl et al. (Biotechnology 5: 720-725, 1987), Handa-Corrigan et al. (Enzyme Microb. Technol. 11: 230-235, 1989), Schneider (J. Immunol. Methods 116: 65-77, 1989) (Schneider et al. 1989), Schneider et al. (J. Immunol. Methods. 129: 251-268, 1990) (Schneider et al. 1990), Murakami et al. (U.S. Patent No. 5,019,499), Wolfe et al. (U.S. Patent No. 5,232,848) Queen et al. (U.S. Patent No. 5,530,101) and Waldmann et al. (U.S. Patent No. 5,846,534) (1449) for the reasons of record.

Applicant's arguments, filed 02/15/2009, have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant argues the following.

The Applicants respectfully traverse this rejection. In relying on KSR, the Examiner ignores the Courts assertion that "it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does," because claimed inventions almost always rely on combinations of elements that are already known./d, at 1741. Furthermore, the Courts warn of "the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning." Id. at 1742.

As discussed in the response made May 2007, the Examiner uses hindsight reconstruction by taking individual elements from each reference and assumes that a skilled artisan at the time the invention was made would have known to use a multiple dose treatment regimen with glycosylated IgG for autoimmune disease. The Examiner goes even further by cobbling together diseases disclosed in the various references to allege that treatment of rheumatoid arthritis would be obvious based on the disclosure of Waldmann, et al. and Queen, et al. The Applicants respectfully submit that the Examiner has chosen individual words from each reference to arrive at the current invention which relates to the treatment of a particular disease, even though in some instances the words are taken out of context.

Additionally, the Examiner incorrectly applies the "common sense" test of KSR to Waldmann, et al. and Queen, et al. to arrive at the present invention. The Applicants refer to Parekh et al. Nature 316:452-457 (1985), submitted previously in a response of May 2007. Parehk, et al. demonstrate that in patient populations of patients having arthritide diseases, such as rheumatoid arthritis or osteoarthritis, IgG molecules of these patients contain truncated glycan chains compared with normal individuals. Parehk, et al. suggest that these two diseases may be "glycosylation diseases." Parehk, et al. further suggest that oligosaccharides terminating in N-acetylglucosmnine (i.e., having a truncated glycan adduct) could create new protein oligosaccharides that may be immunogenic, increase the population of certain IgG subpopulations raising immunogencity to these IgG, or could effectively make the IgG sticky creating an autoaggregation rather than an immune response. Therefore, Parehk, et al. suggest that aberrantly glycosylated IgG might be immunogenic in patients already having arthritic disease. The Applicants, therefore, submit that multiple administration of a glycosylated IgG for the treatment of a disease such as arthritis, at the time the invention was made, might be expected to increase immunogenicity to the IgG. Therefore, "common sense" would provide no motivation to a skilled artisan to treat a disease such as arthritis with a glycosylated IgG and particularly with a multiple dose treatment regimen.

Furthermore, any multiple dose therapy suggested by Queen, et al. is based on the assumption that immunogenicity to a humanized antibody is reduced because it contains fewer foreign sequences in its framework region compared with rodent framework. Queen, et al. make no reference to glycosylation, nor do they provide anything more than a mere recitation of rheumatoid arthritis as a possible disease for treatment. Thus, the Examiner appears to pick individual elements from the cited references to arrive at the present invention even though those elements have no contextual relationship or even a suggestion that one might connect to the other. There is no "common sense" reason why the skilled artisan would combine them. Given the discussion of Parehk, et al. above and made previously, it is unlikely that the skilled artisan at the time the invention was made would have considered using glycosylated IgG for the treatment of arthritis in a multiple dose regimen. In other words, it would have gone against the "common sense" of the skilled artisan.

Applicants respectfully submit that, in view of the forgoing remarks, the Applicants have overcome the rejection of claims 1, 7-10 and 12 under 35 U.S.C. § 103. Accordingly, the Applicants respectfully request withdrawal of these rejections.

With respect to applicant reliance Parekh et al. (Nature 1985), applicant is reminded that the rejection is based upon cited herein and not Parekh et al. Further, it is noted that the date of Parekh et al. precedes the dates of the prior art. Therefore, the prior art teachings of treating an autoimmune disease by Waldmann et al. and Queen et al. and rheumatoid arthritis with antibodies by Queen et al. clearly stands for what they teach, regardless of what issues may have been raised by Parehk et al. in 1985. Furthermore, while Parekh et al. discuss observations associated with intracellular processing and post-secretory degradation of N-linked oligosaccharides in rheumatoid arthritis, Parekh et al. does not discuss any limitations of such observations in terms of antibody treatment for rheumatoid arthritis, nor any limitations of employing CHO cells in producing therapeutic antibodies at the time the invention was made.

With respect to multiple dosing, such dosing would have obvious in view of a therapeutic regiment to treat chronic disease such as rheumatoid arthritis at the time the invention was made. Multiple dosing was not limited or necessarily associated with antibodies produced in CHO cells or glycosylation of therapeutic antibodies.

The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. See MPEP 2144.

While applicant asserts that the examiner has chosen words from the Waldmann et al. and Queen et al. to arrive at a specific disease,

again Waldmann et al. does teach treating autoimmune diseases (e.g., see column 4, paragraph 2) and Queen et al. does teach that rheumatoid arthritis was a known target of recombinant therapeutic antibodies at the time the invention was made (e.g., see Detailed Description of the Invention, including Anti-gamma- IFN Antibodies; see column 19, lines 19-26; column 21, paragraph 1; column 23, paragraph 2; column 26, paragraph 1; column 36, paragraphs 3-5).

The antibodies of the present invention will typically find use individually in treating substantially any disease susceptible to monoclonal antibody-based therapy. In particular, the immunoglobulins can be used for passive immunization or the removal of unwanted cells or antigens, such as by complement mediated lysis, all without substantial immune reactions (e.g., anaphylactic shock) associated with many prior antibodies. For example, where the cell linked to a disease has been identified as IL-2 receptor bearing, then humanized antibodies that bind to the human IL-2 receptor are suitable (see, U.S. Ser. No. 085,707, entitled "Treating Human Malignancies and Disorders," which is incorporated herein by reference). For such a humanized immunoglobulin, typical disease states suitable for treatment include graft versus host disease and transplant rejection in patients undergoing an organ transplant, such as heart, lungs, kidneys, liver, etc. Other diseases include autoimmune diseases, such as Type I diabetes, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, and myasthenia gravis.

See column 19, paragraph 1 of Queen et al.

For example, typical disease states suitable for treatment include graft versus host disease and transplant rejection in patients undergoing an organ transplant, such as heart, lungs, kidneys, liver, etc. Other diseases include autoimmune diseases, such as Type I diabetes, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, and myasthenia gravis.

See column 23, paragraph 2 of Queen et al.

One cannot show non-obviousness by merely asserting that the references do not provide the sufficient elements of obviousness or by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968). See MPEP 2145.

Again, in response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. In re McLaughlin , 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). See MPEP 2145.

Further, the arguments of counsel cannot take the place of evidence in the record. In re Schulze , 145 USPQ 716, 718 (CCPA 1965). See MPEP 716.01(C).

The following is reiterated for applicant's convenience.

The following of record incorporated references to address applicant's previous amended claims.

Adair et al. teach methods of providing for modified antibodies for diagnostic and therapeutic procedures, including specificities for tumor antigens (e.g. page 4, paragraph 5) that have been produced with glycosylation sites in a variety of host cells including CHO cells (See entire document, including Summary of the Invention and the Description of Specific Embodiments of the Invention). Adair et al. Teach the advantages of modifying the glycosylation of such antibodies includes modifying half-life, preserving properties such as activating complement, binding Fc receptors and inducing ADCC (see Background of the Invention on page 2; Summary of the Invention on pages 3-4 and Abstract). Construction of such chimeric or humanized antibodies involve recombinant expression vectors comprising the immunoglobulin heavy or light chain, introducing such vectors into CHO cells , culturing said cells, recovering said glycosylated antibodies and administering said antibodies (e.g. see Description of Specific Embodiments of the Invention).

Adair et al. differs from the claimed methods by not disclosing that the elected invention arthritis as the target of immunotherapy with CHO glycosylated antibodies.

Queen et al. teach methods of producing recombinant antibodies that can be readily produced and that are substantially less immunogenic for treating human disorders (see entire document, including Summary of the Invention and Detailed Description of the Invention), including the treatment of autoimmune diseases such as rheumatoid arthritis (e.g. see column 19, lines 19-26; column 21, paragraph 1; column 23, paragraph 2; column 26, paragraph 1; column 36, paragraphs 3-5). In addition, Queen et al. teach administering about 1 to about 200 mg of antibody per dose, with dosages of from 5 to 25 mg, including single and multiple administration depending on variables such as the severity of the disease and the patient, which would be determined the ordinary artisan, namely the treating physician at the time the invention was made (e.g. see columns 23-24).

Waldmann et al. teach recombinant antibodies, particularly antibodies to CAMPATH-1, to treat autoimmune diseases (see entire document, including Detailed description of the Invention, including Examples).

Adair et al. teach methods of providing for modified antibodies for diagnostic and therapeutic procedures, including specificities for tumor antigens (e.g. page 4, paragraph 5) that have been produced with glycosylation sites in a variety of host cells including CHO cells (See entire document, including Summary of the Invention and the Description of Specific Embodiments of the Invention). Adair et al. teach the advantages of modifying the glycosylation of such antibodies includes modifying half-life, preserving properties such as activating complement, binding Fc receptors and inducing ADCC (see Background of the Invention on page 2; Summary of the Invention on pages 3-4 and Abstract). Construction of such chimeric or humanized antibodies involve recombinant expression vectors comprising the immunoglobulin heavy or light chain, introducing such vectors into CHO cells, culturing said cells, recovering said glycosylated antibodies and administering said antibodies (e.g. see Description of Specific Embodiments of the Invention).

Adair et al. differs from the claimed invention by not teaching the known steps of culturing transfected CHO cells in serum-free medium as well as the known means of suspension / spinning culturing of cells to produce recombinant proteins of interest at the time the invention was made.

Mather et al. teach small scale and large scale production of applying methods of culturing CHO to high densities in order to improve production of recombinant proteins, including the use of serum free media, including the presence of pluronic F68 (see Preparation of Media, particularly column 10, paragraph 1; Tables 3 – 4 and Table A or Example 1; Claim 3) (see entire document, including Background of the Invention, see column 2; Summary of the Invention, column 3; Detailed Description of the Invention and Claims).

Handa-Corrigan et al. teach the use of defined serum-free media as well as the use of the cell protective agent pluronic F-68 in the growth of mammalian cells (See entire document, including Abstract, Results and Discussion and Conclusion).

Similarly, Schneider et al. 1989 disclose the optimization of hybridoma cell growth and antibody secretion in chemically defined serum-free culture media, including the use of pluronic F68 as well as Iscove's media (see entire document, including Abstract, Materials and Methods, Results and Discussion). For example, Schneider et al. 1989 teach that pluronic acid had no toxic effects on hybridoma cells, improved cell growth and increased antibody secretion (see Effect of Pluronic F68 on page 72). Schneider et al. 1989 teach the use of a totally chemically defined medium for the cultivation of cells provides several advantages over the classical serum-containing media (e.g. see Conclusion, including page 76, column 1, paragraph 3).

In addition, Schneider et al. (1989) also teach the use and advantages of using a semi-continuous mode of cultivation in spinner flasks in producing antibodies (see entire document, including Abstract and Conclusion).
Schneider et al. (1990) further provides for optimization of antibody production in spinner flasks (see entire document, including Abstract and Conclusion)

In addition to Schneider et al. 1989 and Schneider et al. 1990,
Murakami et al. (U.S. Patent No. 5,019,499) and Wolfe et al. (U.S. Patent No. 5,232,848) have been applied in this rejection to address applicant's newly amended claims reciting "spinning culture".

Murokami et al. teach the known use of various means of cultivating or culturing cells in vitro using suitable method depending on the case and for the purpose of efficiently producing the desired polypeptide (e.g., see column 3, paragraph 4), including myeloma cells (e.g., see Summary of the Invention on columns 1-2; Detailed Description of the Invention on columns 2-4 and Examples on columns 4-7) as well as serum free media, as well as spinner flasks (e.g., see column 3, paragraph 5).

While Wolfe et al. was focused on a basal nutrient medium suitable for high and low cell density culture,
Wolfe et al. teach the well known use of CHO cells in cell and the production of antibodies in a variety of production modes, such as hollow fiber bioreactors, fermenters, spinner flasks and roller bottles (e.g., see Detailed Description of the Invention, particularly column 4, paragraph 4; column 7, paragraph 3). Here, too, Wolfe et al. teach the well known use of serum-free media as well (e.g., see Background of the Invention, Summary of the Invention and Detailed Description of the Invention).

Zellemeissl et al. teach the expression of biologically active recombinant protein in CHO cells, including the ability to achieve more than 30 splittings (see entire document, including page 721, column 1, paragraph 3).

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Maher et al., Handa-Corrigan et al. and Schneider to those of Adair et al. to grow CHO cells expressing recombinant antibodies, given the advantages of chemically defined serum-free media and pluronic F68 in the growth of mammalian cells, including CHO cells and/or antibody producing cells, particularly for large-scale cultivation of such cells, as taught by the secondary references. The prior art chemically defined media taught by the secondary references teach the components encompassed by the instant claims. Also, Zellemeissl et al. teach that CHO cells expressing and producing biologically active recombinant proteins could readily undergo a number of passages. Given these teachings of small scale and large scale production recombinant proteins in CHO cells over multiple passages, the ordinary artisan would have had both motivation and a reasonable expectation of success that CHO cells could be cultured for multiple passages, which could occur from two months to greater than five months.

Given that the prior art goal was to treat certain disease, including arthritis, with therapeutic antibodies, providing the antibodies with repeated administration, particularly in a chronic disease such as arthritis, was routine to the ordinary artisan at the time the invention was made and therefore obvious in designing such therapeutic regimens for the treatment of arthritis with therapeutic antibodies.

In contrast to applicant's assertions of record that Parekh et al. suggests that multiple administration of a glycosylated IgG for the treatment of a disease such as the elected species arthritis might be expected to increase the immunogenicity to the IgG,
the combined prior art teaching provided sufficient motivation and expectation of success in achieving the claimed dosages, which were well within the purview of effective amounts and the multiple administration of therapeutic antibodies, which would have comprised a two-part dosing regimen, particularly given the chronic nature of many diseases/disorders, including autoimmune diseases such as arthritis.

Also, as pointed out previously, particular parameters such as dosages and modes of administration were well known and recognized as being result-effective variables (i.e., a variable which achieves a recognized result) in therapeutic regimens at the time the invention was made. In turn, the determination of the optimum or workable ranges of said variables might be characterized as routine experimentation.
For example, MPEP 2144.05, including In re Antonie, 195 USPQ 6 (CCPA 1977).
According to Adair et al., a person of ordinary skill in the art would have been motivated to produce CHO glycosylated therapeutic antibodies, given the advantages of ease and control of production of recombinant antibodies and the advantages of such modifications for altering antibody half-life and effector function(s) in human therapy.

Given providing effective amounts of therapeutic antibodies depended upon various parameters such as the nature of the disease and the patient and the desired endpoints associated with a particular disease/patient, the two-part dosing regime recited in claims 9-10 would have been obvious to the ordinary artisan in providing said effective amounts to a patient in need at the time the invention was made. The claimed dosages were well within the purview of effective amounts and the multiple administration of therapeutic antibodies, which would have comprised a two-part dosing regimen, particularly given the chronic nature of many diseases/disorders, including autoimmune diseases such as arthritis. Further, particular parameters such as dosages and modes of administration were well known and recognized as being result-effective variables (i.e., a variable which achieves a recognized result) in therapeutic regimens at the time the invention was made. In turn, the determination of the optimum or workable ranges of said variables might be characterized as routine experimentation.
For example, see MPEP 2144.05 and In re Antonie, 195 USPQ 6 (CCPA 1977).

As to the use of multiple doses of therapeutic antibodies in the treatment of diseases, including in the treatment of arthritis, as opposed to a single doses alone,
it is noted that we find that a the methods of administration of therapeutic antibodies at the time the invention was made was a result effective variable. It has been well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also Merck & Co. v. Biocraft Labs. Inc., 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious).

As single and multiple administration of therapeutic antibodies were are known and practiced by the ordinary artisan at the time the invention was made, it would have been obvious to optimize both the mode of administration as well as dosage amounts taking into account the standard parameters of the nature of the disease and the patient and the desired endpoints associated with a particular disease/patient.

Therefore, the two-part dosing regimes recited in the instant claims were obvious to the ordinary artisan at the time the invention was made.

"When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." KSR Int'l Co. v. Teleflex Inc., 127 S.Ct. 1727, 1742 (2007).

"The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." KSR, 127 S. Ct. at 1739.

This is the case here as indicated previously and in addressing applicant's previous arguments concerning "suspension culture" or applicant's new arguments concerning "spinning culture",
the claims are obvious over the prior art, which clearly taught the use of CHO cells in producing therapeutic antibodies of interest (e.g., see Adair et al.) as well as the use and advantages of serum free media, and pluronic acid in the growth of CHO cells expressing recombinant proteins, including antibodies and/or antibody-producing cells, particularly in large-scale production was known and practiced at the time the invention was made by the ordinary artisan via various known means of cultivating or culturing cells in vitro using a suitable method depending on the case and for the purpose of efficiently producing the desired polypeptide (see secondary references).

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.
In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. In re McLaughlin , 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). See MPEP 2145.

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 550 U.S., 2007 U.S. LEXIS 4745, 2007 WL 1237837, at *12 (2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Given that the prior art goal was to treat certain disease, including arthritis, with therapeutic antibodies, providing the antibodies with repeated administration, particularly in a chronic disease such as rheumatoid arthritis, was routine to the ordinary artisan at the time the invention was made and therefore obvious in designing such therapeutic regimens for the treatment of rheumatoid arthritis with therapeutic antibodies.

In contrast to applicant's assertions that Parehk et al. suggests that multiple administration of a glycosylated IgG for the treatment of a disease such as the elected species arthritis might be expected to increase the immunogenicity to the IgG,

the combined prior art teaching provided sufficient motivation and expectation of success in achieving the claimed dosages, which were well within the purview of effective amounts and the multiple administration of therapeutic antibodies, which would have comprised a two-part dosing regimen, particularly given the chronic nature of many diseases/disorders, including autoimmune diseases such as arthritis.

Also, as pointed out previously, particular parameters such as dosages and modes of administration were well known and recognized as being result-effective variables (i.e., a variable which achieves a recognized result) in therapeutic regimens at the time the invention was made. In turn, the determination of the optimum or workable ranges of said variables might be characterized as routine experimentation.

For example, MPEP 2144.05, including In re Antonie, 195 USPQ 6 (CCPA 1977).

With respect to applicant's assertions concerning the teachings of Adair et al. and Queen et al. individually, once a prima facie case of obviousness has been made the burden of going further is shifted to applicant. In re Keller, 208 USPQ 871, 882 (CCPA 1981). This applicant has not done, but rather merely asserts that the prior art does not provide sufficient suggestion or motivation to employ the claimed antibodies in the treatment of arthritis or any other glycosylation disease and does not address the teachings of the references individually and not their teachings individually or in combination.

One cannot show non-obviousness by merely asserting that the references do not provide the sufficient elements of obviousness or by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968). See MPEP 2145.

Further, the arguments of counsel cannot take the place of evidence in the record. In re Schulze , 145 USPQ 716, 718 (CCPA 1965). See MPEP 716.01(C).

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Queen et al. and Waldmann et al. to those of Adair et al. to obtain CHO glycosylated antibodies to treat autoimmune diseases such as rheumatoid arthritis (e.g., see Queen et al.).

According to Adair et al., a person of ordinary skill in the art would have been motivated to produce CHO glycosylated therapeutic antibodies, given the advantages of ease and control of production of recombinant antibodies and the advantages of such modifications for altering antibody half-life and effector function(s) in human therapy.

Given providing effective amounts of therapeutic antibodies depended upon various parameters such as the nature of the disease and the patient and the desired endpoints associated with a particular disease/patient, the two-part dosing regime recited in claims 9-10 would have been obvious to the ordinary artisan in providing said effective amounts to a patient in need at the time the invention was made. The claimed dosages were well within the purview of effective amounts and the multiple administration of therapeutic antibodies, which would have comprised a two-part dosing regimen, particularly given the chronic nature of many diseases/disorders, including autoimmune diseases such as arthritis. Further, particular parameters such as dosages and modes of administration were well known and recognized as being result-effective variables (i.e., a variable which achieves a recognized result) in therapeutic regimens at the time the invention was made. In turn, the determination of the optimum or workable ranges of said variables might be characterized as routine experimentation. For example, MPEP 2144.05, including In re Antonie, 195 USPQ 6 (CCPA 1977).

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

As to the use of multiple doses of therapeutic antibodies in the treatment of diseases, including in the treatment of arthritis, as opposed to a single doses alone,

it is noted that we find that a the methods of administration of therapeutic antibodies at the time the invention was made was a result effective variable. It has been well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also Merck & Co. v. Biocraft Labs. Inc., 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious).

As single and multiple administration of therapeutic antibodies were are known and practiced by the ordinary artisan at the time the invention was made, it would have been obvious to optimize both the mode of administration as well as dosage amounts taking into account the standard parameters of the nature of the disease and the patient and the desired endpoints associated with a particular disease/patient.

Therefore, the two-part dosing regimen recited in claims was obvious to the ordinary artisan at the time the invention was made.

Applicant's arguments have not been found persuasive.

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1, 7-10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 49-59 of USSN 12/122,123.

Although the instant and copending claims in the recitation of certain ingredients of the serum-free media to be employed in the CHO expression system, the copending claims would anticipate the instant claims. Also, the ingredients of the serum-free media in copending claims appear to be known ingredients for growing therapeutic proteins / antibodies of interest in a CHO expression system.

Although the instant claims recited a two-part dosing regimen for treating rheumatoid arthritis, As to the use of multiple doses of therapeutic antibodies in the treatment of diseases, including in the treatment of arthritis, as opposed to a single doses alone,

it is noted that we find that a the methods of administration of therapeutic antibodies at the time the invention was made was a result effective variable. It has been well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also Merck & Co. v. Biocraft Labs. Inc., 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious).

As single and multiple administration of therapeutic antibodies were are known and practiced by the ordinary artisan at the time the invention was made, it would have been obvious to optimize both the mode of administration as well as dosage amounts taking into account the standard parameters of the nature of the disease and the patient and the desired endpoints associated with a particular disease/patient.

Therefore, the two-part dosing regimes recited in the instant claims were obvious to the ordinary artisan at the time the invention was made.

10. Claims 1, 7-10 and 12 are directed to an invention not patentably distinct from claims 49-59 of commonly assigned USSN 12/122,123 for the reasons above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No., discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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